

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule consisting of a polynucleotide having a nucleotide sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:1 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:1;

(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:2 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:1;

(c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:2 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:1;

(d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:2 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:1;

(e) a polynucleotide encoding a polypeptide of SEQ ID NO:2 or the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:1, having biological activity;

(f) a polynucleotide which is a variant of SEQ ID NO:1;

(g) a polynucleotide which is an allelic variant of SEQ ID NO:1;

(h) a polynucleotide which encodes a species homologue of the sequence depicted in SEQ ID NO:2;

(i) a polynucleotide which represents the complementary sequence (antisense) of SEQ ID NO:1;

(j) a polynucleotide corresponding to nucleotides 323 to 1648 of SEQ ID NO:1, wherein said nucleotides 323 to 1648 encode a polypeptide of SEQ ID NO:2 minus the start codon;

(k) a polynucleotide corresponding to nucleotides 320 to 1648 of SEQ ID NO:1, wherein said nucleotides 320 to 1648 encode a polypeptide of SEQ ID NO:2 including the start codon;

(l) a polynucleotide fragment of SEQ ID NO:3 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:3;

(m) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:4 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:3;

(n) a polynucleotide encoding a polypeptide domain of SEQ ID NO:4 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:3;

(o) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:4 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:3;

(p) a polynucleotide encoding a polypeptide of SEQ ID NO:4 or the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:3, having biological activity;

(q) a polynucleotide which is a variant of SEQ ID NO:3;

(r) a polynucleotide which is an allelic variant of SEQ ID NO:3;

(s) a polynucleotide which encodes a species homologue of the SEQ ID NO:4;

(t) a polynucleotide which represents the complementary sequence (antisense) of SEQ ID NO:3;

(u) a polynucleotide corresponding to nucleotides 264 to 2139 of SEQ ID NO:3, wherein said nucleotides 264 to 2139 encode a polypeptide of SEQ ID NO:4 minus the start codon;

(v) a polynucleotide corresponding to nucleotides 261 to 2139 of SEQ ID NO:3, wherein said nucleotides 261 to 2139 encode a polypeptide of SEQ ID NO:4 including the start codon;

(w) a polynucleotide fragment of SEQ ID NO:5 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:5;

(x) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:6 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: , which is hybridizable to SEQ ID NO:5;

(y) a polynucleotide encoding a polypeptide domain of SEQ ID NO:6 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:5;

(z) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:6 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:5;

(aa) a polynucleotide encoding a polypeptide of SEQ ID NO:6 or the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:5, having biological activity;

(bb) a polynucleotide which is a variant of SEQ ID NO:5;

(cc) a polynucleotide which is an allelic variant of SEQ ID NO:5;

(dd) a polynucleotide which encodes a species homologue of the SEQ ID NO:6;

(ee) a polynucleotide which represents the complementary sequence (antisense) of SEQ ID NO:5;

(ff) a polynucleotide corresponding to nucleotides 694 to 2139 of SEQ ID NO:5, wherein said nucleotides 694 to 2139 encode a polypeptide of SEQ ID NO:6 minus the start codon;

(gg) a polynucleotide corresponding to nucleotides 691 to 1749 of SEQ ID NO:5, wherein said nucleotides 691 to 2139 encode a polypeptide of SEQ ID NO:6 including the start codon;

(hh) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(gg), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding an adapter protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:2, or SEQ ID NO:4 or SEQ ID NO:6, the polypeptide encoded by the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:1 or SEQ ID NO:3 or SEQ ID NO:5.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or the cDNA sequence included in ATCC Deposit No: PTA-2981, which is hybridizable to SEQ ID NO:1 or SEQ ID NO:3 or SEQ ID NO:5.

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1, comprising:

- (a) introducing the vector of claim 7 into the host cell under conditions such that the nucleic acid molecule is maintained in the cell; and
- (b) growing the host cell to allow production of encoded polypeptide.

9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.

(a) a polypeptide fragment of SEQ ID NO:2 or the encoding sequence included in ATCC Deposit No: PTA-2981;

(c) a polypeptide domain of SEQ ID NO:2 or the encoding sequence included in ATCC Deposit No: PTA-2981;

(d) a polypeptide epitope of SEQ ID NO:2 or the encoding sequence included in ATCC Deposit No: PTA-2981;

(e) a full length protein of SEQ ID NO:2 or the encoding sequence included in ATCC Deposit No: PTA-2981;

(f) a variant of SEQ ID NO:2;

(q) an allelic variant of SEQ ID NO:2;

(h) a species homologue of SEQ ID NO:2;

(i) a polypeptide corresponding to amino acids 2 to 443 of SEQ ID NO:2, wherein said amino acids 2 to 443 comprise a polypeptide of SEQ ID NO:2 minus the start methionine;

(j) a polypeptide corresponding to amino acids 1 to 443 of SEQ ID NO:2;

(k) a polypeptide fragment of SEQ ID NO:4 or the encoding sequence included in ATCC Deposit No: PTA-2981;

(I) a polypeptide fragment of SEQ ID NO:4 or the encoding sequence included in ATCC Deposit No: PTA-2981, having biological activity;

(m) a polypeptide domain of SEQ ID NO:4 or the encoding sequence included in ATCC Deposit No: PTA-2981;

(n) a polypeptide epitope of SEQ ID NO:4 or the encoding sequence included in ATCC Deposit No: PTA-2981;

- (o) a full length protein of SEQ ID NO:4 or the encoding sequence included in ATCC Deposit No: PTA-2981;
- (p) a variant of SEQ ID NO:4;
- (q) an allelic variant of SEQ ID NO:4;
- (r) a species homologue of SEQ ID NO:4;
- (s) a polypeptide corresponding to amino acids 2 to 428 of SEQ ID NO:4, wherein said amino acids 2 to 428 comprise a polypeptide of SEQ ID NO:4 minus the start methionine;
- (t) a polypeptide corresponding to amino acids 1 to 428 of SEQ ID NO:4;
- (u) a polypeptide fragment of SEQ ID NO:6 or the encoding sequence included in ATCC Deposit No: PTA-2981;
- (v) a polypeptide fragment of SEQ ID NO:6 or the encoding sequence included in ATCC Deposit No: PTA-2981, having biological activity;
- (w) a polypeptide domain of SEQ ID NO:6 or the encoding sequence included in ATCC Deposit No: PTA-2981;
- (x) a polypeptide epitope of SEQ ID NO:6 or the encoding sequence included in ATCC Deposit No: PTA-2981;
- (y) a full length protein of SEQ ID NO:6 or the encoding sequence included in ATCC Deposit No: PTA-2981;
- (z) a variant of SEQ ID NO:6;
- (aa) an allelic variant of SEQ ID NO:6;
- (bb) a species homologue of SEQ ID NO:6;
- (cc) a polypeptide corresponding to amino acids 2 to 353 of SEQ ID NO:6, wherein said amino acids 2 to 353 comprise a polypeptide of SEQ ID NO:6 minus the start methionine; and
- (dd) a polypeptide corresponding to amino acids 1 to 353 of SEQ ID NO:6.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:
(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and
(b) recovering said polypeptide.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

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21. A method of identifying a biological activity in an assay, wherein the method comprises:
- (a) expressing the MIST sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4 or SEQ ID NO:6 in a host cell under conditions allowing for polypeptide expression; and
 - (b) measuring the resulting activity of the expressed MIST.
22. A method for identifying a binding partner to the polypeptide of claim 11 comprising:
- (a) contacting the polypeptide of claim 11 with a binding partner; and
 - (b) determining whether the binding partner effects an activity of the polypeptide.
23. A method of identifying a compound that modulates the biological activity of MIST, or an adapter protein, comprising:
- (a) combining a candidate modulator compound with a host cell containing a vector according to claim 7, wherein MIST is expressed by the cell; and
 - (c) measuring an effect of the candidate modulator compound on the activity of the expressed MIST.
24. A compound that modulates the biological activity of human MIST as identified by the method according to claim 22 or 23.
25. A method of detecting human MIST SH2-domain-containing adapter protein, or an antibody-reactive fragment thereof, in a sample, comprising:
- (a) contacting the sample with an antibody specific for the polypeptide, or an antigenic fragment thereof, according to claim 11 under conditions in which an antigen-antibody complex can form between the antibody and the polypeptide or antigenic fragment thereof in the sample; and

(b) detecting an antigen-antibody complex formed in step (a), wherein detection of the complex indicates the presence of the human MIST protein, or an antigenic fragment thereof, in the sample.

26. The method according to claim 22 or 23, wherein the candidate compounds are antagonists or inhibitors of human MIST protein.

27. The method according to claim 26, wherein the human MIST activity is binding to an interacting domain of an intracellular cell signaling protein.

28. The method according to claim 27, wherein the intracellular cell signaling protein is Grb2, Vav, LAT, or c-Cbl.

29. A method of treating an immune disorder involving hyperactivity of B- or T-lymphocytes in a mammal comprising administration of the protein according to claim 11 in an amount effective to treat the B- or T-cell hyperactivity.

30. A method of inhibiting growth of or eliminating a T-cell lymphoma, tumor or thymoma in a mammal comprising administration of the polypeptide or homolog according to claim 11 in an amount effective to inhibit the growth of, or eliminate, the T-cell lymphoma, tumor, or thymoma.

31. A method of screening for compounds to identify compounds which enhance, increase, or accelerate binding of human MIST protein with a cell signaling protein, comprising:

(a) contacting human MIST protein according to claim 11 with a cell signaling molecule with which it binds or associates in the presence or absence of a test compound under conditions which permit binding; and

(b) determining if the level of binding of human MIST with the cell signaling molecule is enhanced, increased or accelerated by comparing the level of binding in the presence of the test compound with that in the absence of the test compound.

32. The method according to claim 31, wherein, when Grb2 is the cell signaling molecule that binds to human MIST, antibodies which inhibit MIST/Grb2 binding are included as negative controls.

33. A method of identifying compounds that inhibit the phosphorylation of human MIST by tyrosine kinases, comprising:

- (a) binding human MIST protein according to claim 11 to a solid substrate in a reaction buffer containing ^{32}P -gamma-ATP under conditions to allow binding of human MIST to the substrate;
- (b) adding tyrosine kinase in the presence or absence of a test compound; and
- (c) determining of the presence of the test compound results in a decrease in the amount of ^{32}P label that is incorporated into MIST, compared with the level of phosphorylation observed in the absence of the test compound to identify a test compound that inhibits phosphorylation of human MIST.

34. A gene corresponding to the sequence as set forth in SEQ ID NO:1, or SEQ ID NO:3, or SEQ ID NO:5.

35. A polypeptide corresponding to the sequence as set forth in SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.